

PATENT ABSTRACTS OF JAPAN

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(54) ADIPOSITY INHIBITOR AND PREPARATION FOR EXTERNAL USE FOR SKIN CONTAINING THE SAME

(57)Abstract:

PROBLEM TO BE SOLVED: To obtain the subject inhibitor useful for preparations for external use for skin, exhibiting excellent effect of preventing accumulation of an excessive quantity of fat by controlling increase in number of fat cells and also excellent slimming effect by including an ω -3-based polyunsaturated fatty acid.

SOLUTION: This preparation contains an ω -3-based polyunsaturated fatty acid and/or its derivative (e.g. eicosapentaenoic acid, docosahexaenoic acid and α -linolenic acid) at 0.0001 to 10 wt.%, preferably 0.01 to 5 wt.%, and also preferably contains at least one agent selected from the group consisting of a phosphodiesterase activity inhibitor (e.g. caffeine and theophylline), cyclic AMP and/or its derivative, plant extract containing cyclic AMP (e.g. Jujube extract), β -adrenergic stimulant and/or α 2-adrenergic inhibitor (e.g. isoproterenol), astringent (e.g. aloe extract), blood circulation accelerant (e.g. tocopherol), and lipase activity accelerant (Fucus extract).

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CLAIMS

[Claim(s)]

[Claim 1] The adiposity inhibitor characterized by containing an omega-3 system higher unsaturated fatty acid and/or its derivative.

[Claim 2] The adiposity inhibitor characterized by containing a kind further chosen from a phosphodiesterase activity inhibitor, cyclic AMP and/or its derivative list salt, the plant extract containing cyclic AMP, beta-adrenomimetic analeptic and/or alpha2-adrenomimetic depressant, an astringent, a circulation accelerator, and a lipase activity accelerator, or two sorts or more in addition to a component according to claim 1.

[Claim 3] Skin external preparations characterized by containing claim 1 or an adiposity inhibitor given in either of 2.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the skin external preparations which contain still more useful adiposity inhibitor and this to loss in quantity of the fat tissue of control of obesity or prevention, a part, or the whole body in a detail about an adiposity inhibitor.

[0002]

[Description of the Prior Art] To consumption energy, superfluous intake energy is accumulated as neutral fat into a white fat cell, and arises, and obesity has been a big problem from a viewpoint of medicine or cosmetics regardless of man and woman. Two classes exist in the formation of such obesity. When the capacity of the fat cell which the number of fat cells does not change one, but already exists is expanded, it is the mold (fat cell capacity expansion mold obesity) which holds a fat, and another side is a mold (increment mold obesity in a fat cell) which holds the fat which increases when the number of fat cells increases. Although the expansion of fat cell capacity of the latter increment mold obesity in a fat cell is not remarkable, there is a difficulty of resisting an obesity therapy compared with the former fat cell capacity expansion mold obesity. Although contraction of fat cell capacity takes place comparatively simply, it is because reduction of the number of fat cells does not take place except for the case of being special.

[0003] Using for control of obesity, prevention, and an improvement conventionally cosmetics which promote metabolism in the living body, such as gel for a massage and a cream, in addition to recipe and suitable movement of a diet limit, a drug, etc. is known. As an example, combination of drug effect components, such as caffeine, a Western ivy extract, a hamamelis extract, a green tea extract, a tea extract, an oolong tea extract, and a seaweed extract, was tried by cosmetics aiming at the lean figure effectiveness.

[0004]

[Problem(s) to be Solved by the Invention] However, in the skin external preparations which blended the above-mentioned drug effect component, when the effectiveness of a drug effect component was not enough or blended sufficient amount to obtain drug effect, there are problems -- a feeling of use is spoiled -- and the improvement was desired. Furthermore, the present condition was that the component which acts on the increment mold obesity in a fat cell which the drug effect component which carried out future works on fat cell capacity expansion mold obesity, disassembled the fat, tightens the body by the phosphodiesterase activity inhibitory action and astriction which are one step of lipid metabolism, and set the chief aim to control of the number of fat cells is seldom known. therefore, the increment in the number of fat cells -- controlling -- are recording of a superfluous fat -- protecting -- in addition -- and development of the drug effect component which has sufficient effectiveness was desired strongly.

[0005]

[Means for Solving the Problem] this invention persons came to complete a header and this invention for the skin external preparations excellent in the lean figure effectiveness being obtained having the adiposity depressor effect excellent in an omega-3 system higher unsaturated fatty acid and/or its derivative and that adiposity is controlled in multiplication by combining a specific drug effect component, and by blending further the drug effect agent which has such adiposity depressor effect, as a result of inquiring wholeheartedly. That is, this invention is skin external preparations which contain the adiposity inhibitors containing a kind chosen from a salt, the plant extract containing cyclic AMP, beta-adrenomimetic analeptic and/or alpha2-adrenomimetic depressant, an astringent, a circulation accelerator, and a lipase activity accelerator, or two sorts or more, and these adiposity inhibitors at an omega-3 system higher unsaturated fatty acid and/or its derivative, a phosphodiesterase activity inhibitor and cyclic AMP, and/or its derivative list in the adiposity inhibitor containing an omega-3 system higher unsaturated fatty acid and/or its derivative, and a list. Hereafter, it explains to a detail.

[0006]

[Embodiment of the Invention] Carbon numbers are 18-22, and the numbers of unsaturated bonds of the omega-3 system higher unsaturated fatty acid used for this invention and/or its derivative are three or more free fatty acid and/or a derivative of those. As these free fatty acid, alpha-linolenic acid, a steer RIDON acid, eicosa tetraenoic acid, eicosapentaenoic acid, docosa-hexaenoic acid, etc. are mentioned, for example. Moreover, as these derivatives, it is a salt and ester, and as a salt, amine salts, such as metal salts, such as sodium and a potassium, triethanolamine, and monoethanolamine, etc. are mentioned, and monochrome, JI, triglyceride, etc. with a glycerol are mentioned as ester, for example. Isolating and blending independently can also use these as mixture, and they can use fish oil, sesame oil, etc., such as the fats and oils which contain many these further, for example, a tuna oil, sardine oil, and a Pacific saury oil, as they are.

[0007] In this invention, according to the purpose, a kind of the omega-3 system higher unsaturated fatty acid mentioned above and/or its derivative or two sorts or more can be chosen suitably, and can be used. Also in these, eicosapentaenoic acid (it is hereafter called "EPA" for short), docosa-hexaenoic acid (it is hereafter called "DHA" for short), and alpha-linolenic acid are desirable.

[0008] Although especially the content of the omega-3 system higher unsaturated fatty acid in the constituent of this invention and/or its derivative is not limited, it is 0.0001 - 10 % of the weight ("% only shows hereafter) preferably, and is 0.01 - 5% more preferably. When using an omega-3 system higher unsaturated fatty acid and/or fats and oils with the low purity of the derivative, a real content should just be above-mentioned within the limits. When sufficient effectiveness may not be acquired if the content of an omega-3 system higher unsaturated fatty acid and/or its derivative is less than 0.0001%, and it blends exceeding 10%, the problem in respect of pharmaceutical preparation -- depending on the case, precipitate arises depending on coloring, stinking thing generating, and a pharmaceutical form -- may arise.

[0009] Furthermore, adiposity depressor effect will become more remarkable by combining the omega-3 system higher unsaturated fatty acid mentioned above and/or its derivative, and a specific drug effect component. One sort chosen as a phosphodiesterase activity inhibitor, cyclic AMP, and/or its derivative list from a lipase activity accelerator by a salt, the plant extract containing cyclic AMP, beta-adrenomimetic analeptic and/or an alpha2-adrenomimetic depressant astringent, and the circulation accelerator list as a specific drug effect component or two sorts or more are combined, and, specifically, what is shown below, respectively is mentioned.

[0010] (Phosphodiesterase activity inhibitor) As a phosphodiesterase activity inhibitor, those salts, a citric acid, a tea extract, a green tea extract, an oolong tea extract, etc. are mentioned to the xanthine derivative list represented by caffeine, theophylline, a theobromine, aminophylline, etc., for example, and these kinds or two sorts or more can be chosen suitably, and can be blended.

[0011] As a desirable thing, those salts, a tea extract, a green tea extract, and an oolong tea extract are especially mentioned to caffeine and its derivative list among these phosphodiesterase activity inhibitors at those salts, theophylline, and its derivative list.

[0012] (Plant extract which contains a salt and cyclic AMP in cyclic AMP and/or its derivative list) As a salt, salts, such as derivatives, such as cyclic AMP and dibutyl cyclic AMP, and cyclic AMP sodium, etc. are mentioned, a zizyphi fructus extract etc. is mentioned as a plant extract containing cyclic AMP, and these kinds or two sorts or more can be suitably chosen as cyclic AMP and/or its derivative list, and can be blended with them. They are cyclic AMP and a zizyphi fructus extract especially preferably also in these.

[0013] (beta-adrenomimetic analeptic and/or alpha2-adrenomimetic depressant astringent) As beta-adrenomimetic analeptic and/or an alpha2-adrenomimetic depressant astringent, isoproterenol, the dobutamine, salbutamol, yohimbine, phentolamine, ergotamine, etc. are mentioned, and these kinds or two sorts or more can be chosen suitably, and can be blended.

[0014] (Astringent) As an astringent, a zinc oxide, Para phenolsulfonic acid zinc, a peppermint extract, a cork tree bark extract, a horse chestnut extract, an aloe extract, a hamamelis extract, a rosemary extract, a field horsetail extract, a Western KIZUTA extract, a clematis extract, meadowsweet extract, a lavender extract, a eucalyptus extract, a hop extract, a Betula-alba extract, Bistorta major extract, a butcherbroom extract, etc. are mentioned, and these kinds or two sorts or more can be chosen suitably, and can be blended.

[0015] Especially as for a desirable thing, an aloe extract, a hamamelis extract, a rosemary extract, a field horsetail extract, a Western KIZUTA extract, a clematis extract, meadowsweet extract, a lavender extract, a eucalyptus extract, a hop extract, a Betula-alba extract and Bistorta major extract, a horse chestnut extract, and a butcherbroom extract are mentioned among these astringents.

[0016] (Circulation accelerator) As a circulation accelerator, those salts, gamma-orizanol, camphor, a sialid extract, the

Panax schinseng extract, hinokitiol, a red pepper extract, a ginkgo tree extract, an Arnica extract, a safflower extract, etc. are mentioned to a tocopherol and its derivative, a nicotinic acid, and its derivative list, and these kinds or two sorts or more can be chosen suitably, and can be blended.

[0017] Especially desirable things are those salts, a sialid extract, the Panax schinseng extract, hinokitiol, a red pepper extract, a ginkgo tree extract, a sialid extract, an Arnica extract, and a safflower extract among these circulation accelerators at a tocopherol and its derivative, a nicotinic acid, and its derivative list.

[0018] (Lipase activity accelerator) As a lipase activity accelerator, Fucales extract, a wakame seaweed extract, a Fucus-vesiculosus extract, a green laver extract, a chlorella extract, etc. are mentioned, and these kinds or two sorts or more can be chosen suitably, and can be blended. Especially desirable things are Fucales extract, a chlorella extract, and a wakame seaweed extract among these lipase activity accelerators.

[0019] Although especially the loadings of the drug effect component which is combined with an omega-3 system higher unsaturated fatty acid and/or its derivative and which was mentioned above are not limited, they are 0.01 - 5% more preferably 0.0001 to 10%. If it is this range, the effectiveness of this invention will be more notably discovered.

[0020] As skin external preparations containing the adiposity inhibitor described above, it can consider as the cosmetics for the bodies, quasi drugs, or external use drugs at cosmetics lists, such as a milky lotion, a cream, face toilet, a pack, a charge of washing, and a charge of a massage, for example.

[0021] In the range which does not spoil the effectiveness of this invention, the component blended with the usual skin external preparations other than the above-mentioned indispensable component, for example, oils, fine particles, a surfactant, purified water, polyhydric alcohol, lower alcohol, a high molecular compound, a gelling agent, an ultraviolet ray absorbent, an ultraviolet scattering agent, an antioxidant, coloring matter, antiseptics, perfume, a cosmetics component, etc. can be suitably chosen as the skin external preparations of this invention, and can be used for them.

[0022]

[Example] Next, although the example of a trial and an example are given and this invention is further explained to a detail, this invention is not limited at all by these.

[0023] To the example of trial 1 beginning, the omega-3 system higher unsaturated fatty acid examined about the effect which it has on differentiation of a fat cell. It is known that a fat cell will specialize from the fibroblast called a fat precursor cell. Then, the differentiation accelerator was added to fibroblast, and when it was made to specialize to a fat cell, it evaluated by using as a differentiation manifestation marker the enzyme activated specifically about the effect which omega3 system higher unsaturated fatty acid has on differentiation of a fat cell.

[0024] (The evaluation approach) A cell is made for 0.5×10^5 3 T3-L1 fat precursor cells (fibroblast)/ml to specialize by the 0.5mM1-methyl-3-isobutyl xanthin and 0.25microM dexamethasone after culture for two days in 10%FBS-DMEM culture medium. At this time, omega-3 system higher unsaturated fatty acids are added in a culture medium to coincidence. after 48 more hour culture and 10%FBS-DMEM -- returning -- nine days after seeding -- as the differentiation manifestation marker to a fat cell -- glycerol 3-phosphate dehydrogenase (GPDH) activity -- measuring - coincidence -- Lowly -- the protein quantum was performed by law and specific activity (a unit/mg) was computed. The relative value when making specific activity of control into 100% is shown in Table 1.

[0025]

[Table 1]

(試料)		GPDH活性(対コントロール%)
DHA(注1)	0.01mM(0.0003%)	79.0
	0.1mM(0.003%)	47.0
EPA(注2)	0.01mM(0.0003%)	81.0
	0.1mM(0.003%)	72.0
α -リノレン酸(注3)	0.01mM(0.0003%)	68.0
	0.1mM(0.003%)	63.0

(注1)～(注3)：すべてシグマ社製

[0026] Since the GPDH activity which is all a differentiation manifestation marker to a fat cell fell, by DHA, EPA, and the omega-3 system higher unsaturated fatty acid addition group of alpha-linolenic acid, it became clear to control the differentiation to a fat cell from a fat precursor cell, so that the result of Table 1 might show.

[0027] Examples 1-4 and examples 1-3 of a comparison The cream of the presentation shown in the cream table 2 was prepared, and the lean figure effectiveness was evaluated.

[0028]

[Table 2]

(%)

(成分)	実施例				比較例		
	1	2	3	4	1	2	3
1. ミツロウ	6.0	6.0	6.0	6.0	6.0	6.0	6.0
2. セタノール	5.0	5.0	5.0	5.0	5.0	5.0	5.0
3. 還元ワロシ	5.0	5.0	5.0	5.0	5.0	5.0	5.0
4. ステアリン	30.0	30.0	30.0	30.0	30.0	30.0	30.0
5. グリセリンモノステアレート	4.0	4.0	4.0	4.0	4.0	4.0	4.0
6. 親油性モノステアリン酸セリレン	2.0	2.0	2.0	2.0	2.0	2.0	2.0
7. ポリオキシエチレンソルビタンモノラウレート (20E.O.)	2.0	2.0	2.0	2.0	2.0	2.0	2.0
8. DHA含有油脂(注1)	5.0	5.0	5.0	5.0	—	—	—
9. 紅茶抽出物(注2)	—	0.2	—	0.2	—	0.2	—
10. センブリ抽出物(注3)	—	—	0.2	0.2	—	—	0.2
11. 防腐剤	適量	適量	適量	適量	適量	適量	適量
12. 香料	適量	適量	適量	適量	適量	適量	適量
13. 精製水	残量	残量	残量	残量	残量	残量	残量
(瘦身効果) 体脂肪減少率 (%)	-6.2	-7.8	-8.2	-9.3	+1.5	-2.7	-3.4

(注1) DHA含有量が35%の魚油精製品

(注2) アガティの葉を50v/v%エタノールで抽出したもの

(注3) センブリの全草を無水エタノールで抽出したもの

[0029] (Process)

A: Reach component 1-8, mix and heat 11, and keep at 70 degrees C.

B: Heat a component 13 and keep at 70 degrees C.

C: Add B to A, and cool after carrying out emulsification mixing.

D: C was attained to component 9-10, 12 was added, and the cream was obtained.

[0030] (The evaluation approach) 15 18-28 year-old [per subject cream] women were used as the panel, the optimum dose of a subject cream was applied to the whole body over 1 time and 12 weeks every night after bathing, and it fully massaged. Change of the body fat percentage before and behind the duration of test was measured using the body fat percentage measuring instrument (body fat meter BFT-2000; blanket science company make), it asked for body fat percentage percentage reduction, it was averaged further, and the lean figure effectiveness was evaluated. The obtained result is collectively shown in Table 2.

[0031] The cream which blended the DHA content fats and oils concerning this invention was what has the lean figure effectiveness which decreased the body fat percentage and was excellent by applying to the skin so that clearly from the result of Table 2. Furthermore, the effectiveness of DHA content fats and oils, the phosphodiesterase activity inhibitor, and the cream that blended DHA content fats and oils and a circulation accelerator with the list was more remarkable respectively. The example of a comparison which is the conventional technique which blended the phosphodiesterase activity inhibitor and the circulation accelerator independently to it was not enough as the effectiveness.

[0032]

Example 5 Face toilet (component) (%)

1. Glycerol 3.0 2.1, 3-butylene glycol 2.0 3. polyoxyethylene (20E.O.) sorbitan 1.0 Mono-laurate 4. ethyl alcohol 5.0 5.EPA (notes 1) 0.5 6. Panax schinseng extract (notes 2) 3.0 7. antiseptics optimum dose 8. perfume Optimum dose 9. purified water Residue (notes 1) Sigma company make (notes 2) What extracted the root of Panax schinseng by 90 v/v% ethanol.

[0033] (Process)

A: Carry out the mixed dissolution of the components 3, 4, 5, 7, and 8.

B: Carry out the mixed dissolution of the components 1, 2, 6, and 9.

C. A and B were mixed, it was made homogeneity and face toilet was obtained.

The face toilet of an example 5 showed the outstanding lean figure effectiveness.

[0034]

Example 6 Milky lotion (component) (%)

1. Polyoxyethylene (10E.O.) Sorbitan 1.0 Monostearate 2. polyoxyethylene (60E.O.) sorbitan 0.5 Tetra-oleate 3. glyceryl monostearate 1.0 4. stearic acid 0.5 5. behenyl alcohol 0.56. Squalane 8.0 7. alpha-linolenic acid (notes 1) 2.08. Caffeine 0.1 (notes 2) 9. zizyphi fructus extract (notes 3) 0.110. Fucales extract (notes 4) 0.111. Antiseptics Optimum dose 12. carboxyvinyl polymer 0.113. Sodium hydroxide 0.0514. ethyl alcohol 5.015. purified water Residue 16. perfume Optimum dose (notes 1) Sigma company make (notes 2) The Kanto chemistry company make (notes 3) What extracted the fruits of zizyphi fructus with purified water.

(Notes 4) What extracted the stem of the vegetation of Fucus by 90 v/v% ethanol.

[0035] (Process)

A: Carry out heating mixing of the components 8-15, and keep at 70 degrees C.

B: Carry out heating mixing of the components 1-7, and keep at 70 degrees C.

C: Add A to B and carry out emulsification mixing.

D: A part for the cooling epigenesis 16 was added, C was mixed to homogeneity, and the milky lotion was obtained.

The milky lotion of an example 6 showed the outstanding lean figure effectiveness.

[0036]

Example 7 Gel for a massage (component) (%)

1. Ethanol 10.0 2. polyoxyethylene (60) hydrogenated castor oil 0.5 3. carboxyvinyl polymer 0.5 4. triethanolamine 0.5 5. glycerol 10.0 6. dipropylene glycol 5.0 7.DHA content fats and oils (notes 1) 5.0 8. isopropanol tele roll (notes 2) 0.02 9. antiseptics Optimum dose 10. perfume Optimum dose 11. purified water Optimum dose (notes 1) Fish oil refined material whose DHA content is 35% (notes 2) Sigma company make [0037] (Process)

A: Carry out heating mixing of the components 1, 2, 9, and 10, and keep at 75 degrees C.

B: Carry out heating mixing of components 3-8 and the component 11, and keep at 75 degrees C.

C: Add A to B.

D: C was cooled and the gel for a massage was obtained.

The gel for a massage of an example 7 showed the outstanding lean figure effectiveness.

[0038]

Example 8 Pack (component) (%)

1. Polyvinyl Alcohol 20.0 2. ethyl alcohol 20.0 3. glycerol 5.0 4. kaolin 6.0 5.EPA content fats and oils (notes 1) 1.0 6. horse chestnut extract (notes 2) 3.0 7. antiseptics optimum dose 8. perfume Optimum dose 9. purified water Residue (notes 1) Fish oil refined material whose EPA content is 25% (notes 2) What extracted the dried fruit of a horse chestnut by 1 and 3-butylene glycol.

[0039] (Process)

A: Mix components 1, 3, 4, 6, and 9, and heat and stir at 70 degrees C.

B: Mix components 2, 5, 7, and 8.

C: It cooled and the pack was obtained, after adding B to A and mixing.

The pack of an example 8 showed the outstanding lean figure effectiveness.

[0040]

Example 9 Charge of washing (component) (%)

1. Stearic Acid 10.0 2. palmitic acid 8.0 3. myristic acid 12.0 4. lauric acid 4.0 5. oleyl alcohol 1.5 6. purified lanolin 1.0 7. perfume Optimum dose 8. antiseptics Optimum dose 9. glycerol 18.010. potassium hydroxide 6.011. DHA content fats and oils (notes 1) 5.012. Acetic-acid-dl-alpha-tocopherol (notes 2) 0.0513. purified water Residue (notes 1) Fish oil refined material whose DHA content is 25% (notes 2) Made in Tokyo Chemicals [0041] (Process)

A: Mix components 9, 10, and 13 and heat at 70 degrees C.

B: Mix components 1-6, and 8, 11 and 12, and heat at 70 degrees C.

C: B was added to A, and it kept at 70 degrees C for a while, and cooled to 50 degrees C after completing a saponification reaction, and the component 7 was added, it cooled, and the charge of washing was obtained.

The charge of washing of an example 9 showed the outstanding lean figure effectiveness.

[0042]

[Effect of the Invention] The adiposity inhibitor of this invention is excellent in the effectiveness which controls the differentiation to a fat cell from a fat precursor cell, controls the increment in the number of fat cells, and prevents are recording of a superfluous fat. Furthermore, the skin external preparations containing this adiposity inhibitor have the outstanding lean figure effectiveness, and are very useful in cosmetics or medicine.

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TECHNICAL FIELD

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PRIOR ART

[Description of the Prior Art] To consumption energy, superfluous intake energy is accumulated as neutral fat into a white fat cell, and arises, and obesity has been a big problem from a viewpoint of medicine or cosmetics regardless of man and woman. Two classes exist in the formation of such obesity. When the capacity of the fat cell which the number of fat cells does not change one, but already exists is expanded, it is the mold (fat cell capacity expansion mold obesity) which holds a fat, and another side is a mold (increment mold obesity in a fat cell) which holds the fat which increases when the number of fat cells increases. Although the expansion of fat cell capacity of the latter increment mold obesity in a fat cell is not remarkable, there is a difficulty of resisting an obesity therapy compared with the former fat cell capacity expansion mold obesity. Although contraction of fat cell capacity takes place comparatively simply, it is because reduction of the number of fat cells does not take place except for the case of being special. [0003] Using for control of obesity, prevention, and an improvement conventionally cosmetics which promote metabolism in the living body, such as gel for a massage and a cream, in addition to recipe and suitable movement of a diet limit, a drug, etc. is known. As an example, combination of drug effect components, such as caffeine, a Western ivy extract, a hamamelis extract, a green tea extract, a tea extract, an oolong tea extract, and a seaweed extract, was tried by cosmetics aiming at the lean figure effectiveness.

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EFFECT OF THE INVENTION

[Effect of the Invention] The adiposity inhibitor of this invention is excellent in the effectiveness which controls the differentiation to a fat cell from a fat precursor cell, controls the increment in the number of fat cells, and prevents are recording of a superfluous fat. Furthermore, the skin external preparations containing this adiposity inhibitor have the outstanding lean figure effectiveness, and are very useful in cosmetics or medicine.

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TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] However, in the skin external preparations which blended the above-mentioned drug effect component, when the effectiveness of a drug effect component was not enough or blended sufficient amount to obtain drug effect, there are problems -- a feeling of use is spoiled -- and the improvement was desired. Furthermore, the present condition was that the component which acts on the increment mold obesity in a fat cell which the drug effect component which carried out future works on fat cell capacity expansion mold obesity, disassembled the fat, tightens the body by the phosphodiesterase activity inhibitory action and astriction which are one step of lipid metabolism, and set the chief aim to control of the number of fat cells is seldom known. therefore, the increment in the number of fat cells -- controlling -- are recording of a superfluous fat -- protecting -- in addition -- and development of the drug effect component which has sufficient effectiveness was desired strongly.

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MEANS

[Means for Solving the Problem] this invention persons came to complete a header and this invention for the skin external preparations excellent in the lean figure effectiveness being obtained having the adiposity depressor effect excellent in an omega-3 system higher unsaturated fatty acid and/or its derivative and that adiposity is controlled in multiplication by combining a specific drug effect component, and by blending further the drug effect agent which has such adiposity depressor effect, as a result of inquiring wholeheartedly. That is, this invention is skin external preparations which contain the adiposity inhibitors containing a kind chosen from a salt, the plant extract containing cyclic AMP, beta-adrenomimetic analeptic and/or alpha2-adrenomimetic depressant, an astringent, a circulation accelerator, and a lipase activity accelerator, or two sorts or more, and these adiposity inhibitors at an omega-3 system higher unsaturated fatty acid and/or its derivative, a phosphodiesterase activity inhibitor and cyclic AMP, and/or its derivative list in the adiposity inhibitor containing an omega-3 system higher unsaturated fatty acid and/or its derivative, and a list. Hereafter, it explains to a detail.

[0006]

[Embodiment of the Invention] Carbon numbers are 18-22, and the numbers of unsaturated bonds of the omega-3 system higher unsaturated fatty acid used for this invention and/or its derivative are three or more free fatty acid and/or a derivative of those. As these free fatty acid, alpha-linolenic acid, a steer RIDON acid, eicosa tetraenoic acid, eicosapentaenoic acid, docosa-hexaenoic acid, etc. are mentioned, for example. Moreover, as these derivatives, it is a salt and ester, and as a salt, amine salts, such as metal salts, such as sodium and a potassium, triethanolamine, and monoethanolamine, etc. are mentioned, and monochrome, JI, triglyceride, etc. with a glycerol are mentioned as ester, for example. Isolating and blending independently can also use these as mixture, and they can use fish oil, sesame oil, etc., such as the fats and oils which contain many these further, for example, a tuna oil, sardine oil, and a Pacific saury oil, as they are.

[0007] In this invention, according to the purpose, a kind of the omega-3 system higher unsaturated fatty acid mentioned above and/or its derivative or two sorts or more can be chosen suitably, and can be used. Also in these, eicosapentaenoic acid (it is hereafter called "EPA" for short), docosa-hexaenoic acid (it is hereafter called "DHA" for short), and alpha-linolenic acid are desirable.

[0008] Although especially the content of the omega-3 system higher unsaturated fatty acid in the constituent of this invention and/or its derivative is not limited, it is 0.0001 - 10 % of the weight ("% only shows hereafter) preferably, and is 0.01 - 5% more preferably. When using an omega-3 system higher unsaturated fatty acid and/or fats and oils with the low purity of the derivative, a real content should just be above-mentioned within the limits. When sufficient effectiveness may not be acquired if the content of an omega-3 system higher unsaturated fatty acid and/or its derivative is less than 0.0001%, and it blends exceeding 10%, the problem in respect of pharmaceutical preparation -- depending on the case, precipitate arises depending on coloring, stinking thing generating, and a pharmaceutical form -- may arise.

[0009] Furthermore, adiposity depressor effect will become more remarkable by combining the omega-3 system higher unsaturated fatty acid mentioned above and/or its derivative, and a specific drug effect component. One sort chosen as a phosphodiesterase activity inhibitor, cyclic AMP, and/or its derivative list from a lipase activity accelerator by a salt, the plant extract containing cyclic AMP, beta-adrenomimetic analeptic and/or an alpha2-adrenomimetic depressant astringent, and the circulation accelerator list as a specific drug effect component or two sorts or more are combined, and, specifically, what is shown below, respectively is mentioned.

[0010] (Phosphodiesterase activity inhibitor) As a phosphodiesterase activity inhibitor, those salts, a citric acid, a tea extract, a green tea extract, an oolong tea extract, etc. are mentioned to the xanthine derivative list represented by caffeine, theophylline, a theobromine, aminophylline, etc., for example, and these kinds or two sorts or more can be

chosen suitably, and can be blended.

[0011] As a desirable thing, those salts, a tea extract, a green tea extract, and an oolong tea extract are especially mentioned to caffeine and its derivative list among these phosphodiesterase activity inhibitors at those salts, theophylline, and its derivative list.

[0012] (Plant extract which contains a salt and cyclic AMP in cyclic AMP and/or its derivative list) As a salt, salts, such as derivatives, such as cyclic AMP and dibutyryl cyclic AMP, and cyclic AMP sodium, etc. are mentioned, a zizyphi fructus extract etc. is mentioned as a plant extract containing cyclic AMP, and these kinds or two sorts or more can be suitably chosen as cyclic AMP and/or its derivative list, and can be blended with them. They are cyclic AMP and a zizyphi fructus extract especially preferably also in these.

[0013] (beta-adrenomimetic analeptic and/or alpha2-adrenomimetic depressant astringent) As beta-adrenomimetic analeptic and/or an alpha2-adrenomimetic depressant astringent, isoproterenol, the dobutamine, salbutamol, yohimbine, phentolamine, ergotamine, etc. are mentioned, and these kinds or two sorts or more can be chosen suitably, and can be blended.

[0014] (Astringent) As an astringent, a zinc oxide, Para phenolsulfonic acid zinc, a peppermint extract, a cork tree bark extract, a horse chestnut extract, an aloe extract, a hamamelis extract, a rosemary extract, a field horsetail extract, a Western KIZUTA extract, a clematis extract, meadowsweet extract, a lavender extract, a eucalyptus extract, a hop extract, a Betula-alba extract, Bistorta major extract, a butcherbroom extract, etc. are mentioned, and these kinds or two sorts or more can be chosen suitably, and can be blended.

[0015] Especially as for a desirable thing, an aloe extract, a hamamelis extract, a rosemary extract, a field horsetail extract, a Western KIZUTA extract, a clematis extract, meadowsweet extract, a lavender extract, a eucalyptus extract, a hop extract, a Betula-alba extract and Bistorta major extract, a horse chestnut extract, and a butcherbroom extract are mentioned among these astringents.

[0016] (Circulation accelerator) As a circulation accelerator, those salts, gamma-orizanol, camphor, a sialid extract, the Panax schinseng extract, hinokitiol, a red pepper extract, a ginkgo tree extract, an Arnica extract, a safflower extract, etc. are mentioned to a tocopherol and its derivative, a nicotinic acid, and its derivative list, and these kinds or two sorts or more can be chosen suitably, and can be blended.

[0017] Especially desirable things are those salts, a sialid extract, the Panax schinseng extract, hinokitiol, a red pepper extract, a ginkgo tree extract, a sialid extract, an Arnica extract, and a safflower extract among these circulation accelerators at a tocopherol and its derivative, a nicotinic acid, and its derivative list.

[0018] (Lipase activity accelerator) As a lipase activity accelerator, Fucales extract, a wakame seaweed extract, a Fucus-vesiculosus extract, a green laver extract, a chlorella extract, etc. are mentioned, and these kinds or two sorts or more can be chosen suitably, and can be blended. Especially desirable things are Fucales extract, a chlorella extract, and a wakame seaweed extract among these lipase activity accelerators.

[0019] Although especially the loadings of the drug effect component which is combined with an omega-3 system higher unsaturated fatty acid and/or its derivative and which was mentioned above are not limited, they are 0.01 - 5% more preferably 0.0001 to 10%. If it is this range, the effectiveness of this invention will be more notably discovered.

[0020] As skin external preparations containing the adiposity inhibitor described above, it can consider as the cosmetics for the bodies, quasi drugs, or external use drugs at cosmetics lists, such as a milky lotion, a cream, face toilet, a pack, a charge of washing, and a charge of a massage, for example.

[0021] In the range which does not spoil the effectiveness of this invention, the component blended with the usual skin external preparations other than the above-mentioned indispensable component, for example, oils, fine particles, a surfactant, purified water, polyhydric alcohol, lower alcohol, a high molecular compound, a gelling agent, an ultraviolet ray absorbent, an ultraviolet scattering agent, an antioxidant, coloring matter, antiseptics, perfume, a cosmetics component, etc. can be suitably chosen as the skin external preparations of this invention, and can be used for them.

[Translation done.]

* NOTICES *

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- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.**** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

EXAMPLE

[Example] Next, although the example of a trial and an example are given and this invention is further explained to a detail, this invention is not limited at all by these.

[0023] To the example of trial 1 beginning, the omega-3 system higher unsaturated fatty acid examined about the effect which it has on differentiation of a fat cell. It is known that a fat cell will specialize from the fibroblast called a fat precursor cell. Then, the differentiation accelerator was added to fibroblast, and when it was made to specialize to a fat cell, it evaluated by using as a differentiation manifestation marker the enzyme activated specifically about the effect which omega3 system higher unsaturated fatty acid has on differentiation of a fat cell.

[0024] (The evaluation approach) A cell is made for 0.5×10^5 3 T3-L1 fat precursor cells (fibroblast)/ml to specialize by the 0.5mM 1-methyl-3-isobutyl xanthin and 0.25microM dexamethasone after culture for two days in 10%FBS-DMEM culture medium. At this time, omega-3 system higher unsaturated fatty acids are added in a culture medium to coincidence. after 48 more hour culture and 10%FBS-DMEM -- returning -- nine days after seeding -- as the differentiation manifestation marker to a fat cell -- glycerol 3-phosphate dehydrogenase (GPDH) activity -- measuring - - coincidence -- Lowly -- the protein quantum was performed by law and specific activity (a unit/mg) was computed. The relative value when making specific activity of control into 100% is shown in Table 1.

[0025]

[Table 1]

(試料)		GPDH活性(対コントロール%)
DHA(注1)	0.01mM(0.0003%)	79.0
	0.1mM(0.003%)	47.0
EPA(注2)	0.01mM(0.0003%)	81.0
	0.1mM(0.003%)	72.0
α -リノレン酸(注3)	0.01mM(0.0003%)	68.0
	0.1mM(0.003%)	63.0

(注1)～(注3)：すべてシグマ社製

[0026] Since the GPDH activity which is all a differentiation manifestation marker to a fat cell fell, by DHA, EPA, and the omega-3 system higher unsaturated fatty acid addition group of alpha-linolenic acid, it became clear to control the differentiation to a fat cell from a fat precursor cell, so that the result of Table 1 might show.

[0027] Examples 1-4 and examples 1-3 of a comparison The cream of the presentation shown in the cream table 2 was prepared, and the lean figure effectiveness was evaluated.

[0028]

[Table 2]

(%)

(成分)	実施例				比較例		
	1	2	3	4	1	2	3
1. ミツロウ	6.0	6.0	6.0	6.0	6.0	6.0	6.0
2. セタノール	5.0	5.0	5.0	5.0	5.0	5.0	5.0
3. 還元ワラン	5.0	5.0	5.0	5.0	5.0	5.0	5.0
4. ステアリン	30.0	30.0	30.0	30.0	30.0	30.0	30.0
5. グリセリンモノステアレート	4.0	4.0	4.0	4.0	4.0	4.0	4.0
6. 親油性モノステアリン酸グリセリン	2.0	2.0	2.0	2.0	2.0	2.0	2.0
7. ポリオキシエチレンポリビタ モノラレート(20E.O.)	2.0	2.0	2.0	2.0	2.0	2.0	2.0
8. DHA含有油脂(注1)	5.0	5.0	5.0	5.0	—	—	—
9. 紅茶抽出物(注2)	—	0.2	—	0.2	—	0.2	—
10. センブリ抽出物(注3)	—	—	0.2	0.2	—	—	0.2
11. 防腐剤	適量	適量	適量	適量	適量	適量	適量
12. 香料	適量	適量	適量	適量	適量	適量	適量
13. 精製水	残量	残量	残量	残量	残量	残量	残量
(瘦身効果) 体脂肪減少率 (%)	-6.2	-7.8	-8.2	-9.3	+1.5	-2.7	-3.4

(注1) DHA含有量が35%の魚油精製品

(注2) アガティの葉を50v/v%エタノールで抽出したもの

(注3) センブリの全草を無水エタノールで抽出したもの

[0029] (Process)

A: Reach component 1-8, mix and heat 11, and keep at 70 degrees C.

B: Heat a component 13 and keep at 70 degrees C.

C: Add B to A, and cool after carrying out emulsification mixing.

D: C was attained to component 9-10, 12 was added, and the cream was obtained.

[0030] (The evaluation approach) 15 18-28 year-old [per subject cream] women were used as the panel, the optimum dose of a subject cream was applied to the whole body over 1 time and 12 weeks every night after bathing, and it fully massaged. Change of the body fat percentage before and behind the duration of test was measured using the body fat percentage measuring instrument (body fat meter BFT-2000; blanket science company make), it asked for body fat percentage percentage reduction, it was averaged further, and the lean figure effectiveness was evaluated. The obtained result is collectively shown in Table 2.

[0031] The cream which blended the DHA content fats and oils concerning this invention was what has the lean figure effectiveness which decreased the body fat percentage and was excellent by applying to the skin so that clearly from the result of Table 2. Furthermore, the effectiveness of DHA content fats and oils, the phosphodiesterase activity inhibitor, and the cream that blended DHA content fats and oils and a circulation accelerator with the list was more remarkable respectively. The example of a comparison which is the conventional technique which blended the phosphodiesterase activity inhibitor and the circulation accelerator independently to it was not enough as the effectiveness.

[0032]

Example 5 Face toilet (component) (%)

1. Glycerol 3.0 2.1, 3-butylene glycol 2.0 3. polyoxyethylene (20E.O.) sorbitan 1.0 Mono-laurate 4. ethyl alcohol 5.0 5.EPA (notes 1) 0.5 6. Panax schinseng extract (notes 2) 3.0 7. antiseptics optimum dose 8. perfume Optimum dose 9. purified water Residue (notes 1) Sigma company make (notes 2) What extracted the root of Panax schinseng by 90 v/v% ethanol.

[0033] (Process)

A: Carry out the mixed dissolution of the components 3, 4, 5, 7, and 8.

B: Carry out the mixed dissolution of the components 1, 2, 6, and 9.

C. A and B were mixed, it was made homogeneity and face toilet was obtained.

The face toilet of an example 5 showed the outstanding lean figure effectiveness.

[0034]

Example 6 Milky lotion (component) (%)

1. Polyoxyethylene (10E.O.) Sorbitan 1.0 Monostearate 2. polyoxyethylene (60E.O.) sorbitan 0.5 Tetra-oleate 3.

glyceryl monostearate 1.0 4. stearic acid 0.5 5. behenyl alcohol 0.5 6. squalane 8.0 7. alpha-linolenic acid (notes 1) 2.08. Caffeine (notes 2) 0.1 9. zizyphi fructus extract (notes 3) 0.1 10. Fucal extract (notes 4) 0.1 11. Antiseptics Optimum dose 12. carboxyvinyl polymer 0.1 13. Sodium hydroxide 0.05 14. ethyl alcohol 5.0 15. purified water Residue 16. perfume Optimum dose (notes 1) Sigma company make (notes 2) The Kanto chemistry company make (notes 3) What extracted the fruits of zizyphi fructus with purified water.

(Notes 4) What extracted the stem of the vegetation of Fucus by 90 v/v% ethanol.

[0035] (Process)

A: Carry out heating mixing of the components 8-15, and keep at 70 degrees C.

B: Carry out heating mixing of the components 1-7, and keep at 70 degrees C.

C: Add A to B and carry out emulsification mixing.

D: A part for the cooling epigenesis 16 was added, C was mixed to homogeneity, and the milky lotion was obtained. The milky lotion of an example 6 showed the outstanding lean figure effectiveness.

[0036]

Example 7 Gel for a massage (component) (%)

1. Ethanol 10.0 2. polyoxyethylene (60) hydrogenated castor oil 0.5 3. carboxyvinyl polymer 0.5 4. triethanolamine 0.5 5. glycerol 10.0 6. dipropylene glycol 5.0 7. DHA content fats and oils (notes 1) 5.0 8. isopropanol tele roll (notes 2) 0.02 9. antiseptics Optimum dose 10. perfume Optimum dose 11. purified water Optimum dose (notes 1) Fish oil refined material whose DHA content is 35% (notes 2) Sigma company make [0037] (Process)

A: Carry out heating mixing of the components 1, 2, 9, and 10, and keep at 75 degrees C.

B: Carry out heating mixing of components 3-8 and the component 11, and keep at 75 degrees C.

C: Add A to B.

D: C was cooled and the gel for a massage was obtained.

The gel for a massage of an example 7 showed the outstanding lean figure effectiveness.

[0038]

Example 8 Pack (component) (%)

1. Polyvinyl Alcohol 20.0 2. ethyl alcohol 20.0 3. glycerol 5.0 4. kaolin 6.0 5. EPA content fats and oils (notes 1) 1.0 6. horse chestnut extract (notes 2) 3.0 7. antiseptics optimum dose 8. perfume Optimum dose 9. purified water Residue (notes 1) Fish oil refined material whose EPA content is 25% (notes 2) What extracted the dried fruit of a horse chestnut by 1 and 3-butylene glycol.

[0039] (Process)

A: Mix components 1, 3, 4, 6, and 9, and heat and stir at 70 degrees C.

B: Mix components 2, 5, 7, and 8.

C: It cooled and the pack was obtained, after adding B to A and mixing.

The pack of an example 8 showed the outstanding lean figure effectiveness.

[0040]

Example 9 Charge of washing (component) (%)

1. Stearic Acid 10.0 2. palmitic acid 8.0 3. myristic acid 12.0 4. lauric acid 4.0 5. oleyl alcohol 1.5 6. purified lanolin 1.0 7. perfume Optimum dose 8. antiseptics Optimum dose 9. glycerol 18.0 10. potassium hydroxide 6.0 11. DHA content fats and oils (notes 1) 5.0 12. Acetic-acid-dl-alpha-tocopherol (notes 2) 0.05 13. purified water Residue (notes 1) Fish oil refined material whose DHA content is 25% (notes 2) Made in Tokyo Chemicals [0041] (Process)

A: Mix components 9, 10, and 13 and heat at 70 degrees C.

B: Mix components 1-6, and 8, 11 and 12, and heat at 70 degrees C.

C: B was added to A, and it kept at 70 degrees C for a while, and cooled to 50 degrees C after completing a saponification reaction, and the component 7 was added, it cooled, and the charge of washing was obtained.

The charge of washing of an example 9 showed the outstanding lean figure effectiveness.

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(54) 【発明の名称】 脂肪蓄積抑制剤及びそれを含有する皮膚外用剤

(57) 【要約】

【課題】 脂肪細胞数の増加を抑制して過剰な脂肪の蓄積を防ぐ効果に優れた脂肪細胞蓄積抑制剤、並びにそれを配合することにより優れた瘦身効果を有する皮膚外用剤を提供する。

【解決手段】 ω -3系高度不飽和脂肪酸及び／又はその誘導体を含有することを特徴とする脂肪蓄積抑制剤、さらにそれに特定薬効成分を含有する脂肪蓄積抑制剤、及びそれを含有する皮膚外用剤。